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Registration Decision RD2012-20

Bacillus firmus Strain I-1582

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Registration Decision for *Bacillus firmus* strain I-1582

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of *Bacillus firmus* GB126 Technical Nematicide and Votivo 240 FS Nematicide, containing the technical grade active ingredient *Bacillus firmus* strain I-1582, to suppress certain soil nematodes in soybean and corn seeds.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document[1] Proposed Registration Decision PRD2011-24, *Bacillus firmus* strain I-1582. This Registration Decision[2] describes this stage of the PMRA's regulatory process for *Bacillus firmus* strain I-1582 and summarizes the Agency's decision, the reasons for it and provides, in Appendix I, a summary of comments received during the consultation process as well as the PMRA's response to these comments. This decision is consistent with the proposed registration decision stated in PRD2011-24, *Bacillus firmus* strain I-1582.

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2011-24 - *Bacillus firmus* strain I-1582 that contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[3] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of *Pest Control Products Act*".the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What Is *Bacillus firmus* strain I-1582?

Bacillus firmus strain I-1582 is a soil bacterium that degrades the eggs of certain nematode species, most likely through the action of extracellular enzymes. Other mechanisms may be involved in the nematicidal activity of the bacterium.

Health Considerations

Can Approved Uses of *Bacillus firmus* strain I-1582 Affect Human Health?

Bacillus firmus strain I-1582 is unlikely to affect your health when Votivo 240 FS Nematicide is used according to the label directions.

As the end-use product, Votivo 240 FS Nematicide, is a seed treatment, exposure to *Bacillus firmus* strain I-1582 occurs mainly during handling and applying the product.

When assessing health risks, several key factors are considered:

- the microorganism's biological properties (for example, production of toxic byproducts);
- reports of any adverse incidents;
- its potential to cause disease or toxicity as determined in toxicological studies; and
- the levels to which people may be exposed relative to exposures already encountered in nature to other isolates of this microorganism.

Toxicological studies in laboratory animals describe potential health effects from large doses in order to identify any potential pathogenicity, infectivity and toxicity concerns.

When *Bacillus firmus* strain I-1582 was tested on laboratory animals, there were no signs that it caused any toxicity or disease. Votivo 240 FS Nematicide was mildly irritating to the skin and eyes.

Like all bacteria, *Bacillus firmus* strain I-1582 contains substances that can cause allergic reactions in people who are repeatedly exposed to it at high concentrations. However, these reactions can be avoided if workers and applicators follow label recommendations to minimize or limit exposure to Votivo 240 FS Nematicide.

Residues in Water and Food

Dietary risks from food and water are not of concern.

As part of the assessment process prior to the registration of a pesticide, Health Canada must determine whether the consumption of the maximum amount of residues, that are expected to remain on food products when a pesticide is used according to label directions, will not be a concern to human health. This maximum amount of residues expected is then legally established as a maximum residue limit (MRL) under the *Pest Control Products Act* for the purposes of the adulteration provision of the *Food and Drugs Act*. Health Canada sets science-based MRLs to ensure the food Canadians eat is safe.

Since Votivo 240 FS Nematicide is applied as a seed treatment, residues of *Bacillus firmus* strain I-1582 are not expected to be a concern on corn and soybeans at the time of harvest. As *Bacillus firmus* strains are common in soil, the use of Votivo 240 FS Nematicide is not expected to significantly increase the natural environmental background levels of this microorganism. Also, no adverse effects have been attributed to dietary exposure from natural populations of *Bacillus firmus* strain I-1582, and no adverse effects were observed in the acute oral toxicity study with *Bacillus firmus* strain I-1582. Therefore, the establishment of a maximum residue limit is not required for *Bacillus firmus* strain I-1582. As well, the likelihood of residues contaminating drinking water supplies is negligible to non-existent. Consequently, dietary risks are minimal to non-existent.

Occupational Risks From Handling Votivo 240 FS Nematicide

Occupational risks are not of concern when Votivo 240 FS Nematicide is used according to label directions, which include protective measures.

Workers using Votivo 240 FS Nematicide can come into direct contact with *Bacillus firmus* strain I-1582 on the skin, in the eyes, or by inhalation. For this reason, the label will specify that users exposed to Votivo 240 FS Nematicide must wear personal protective equipment, including a long-sleeved shirt, long pants, shoes plus socks, water-proof gloves, and a dust/mist filtering respirator (MSH/NIOSH approval number prefix TC-21C) or a NIOSH approved respirator with any N-95, R-95, P-95 or HE filter for biological products.

For bystanders, exposure is expected to be much less than that of workers involved in mixing and application activities and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Votivo 240 FS Nematicide Is Introduced Into the Environment?

Environmental risks are not of concern.

Following application, *Bacillus firmus* strain I-1582 is likely able to survive in the environment under favourable environmental conditions (i.e. temperature, humidity) but over time populations of *B. firmus* strain I-1582 are expected to return to natural background levels.

Studies were conducted to determine the effects of *B. firmus* strain I-1582 spores on birds, and terrestrial and aquatic invertebrates. These studies showed that *B. firmus* strain I-1582 was not toxic to the Northern Bobwhite quail and honey bees from oral/dietary exposure and no adverse effects were noted for daphnids.

Although avian pulmonary/inhalation/injection, wild mammal, fish, aquatic insect, earthworm, and microorganism testing were not conducted, adequate information was available to determine that significant adverse effects to these non-target organisms are not expected. There are no published reports of disease associated with *B. firmus* strain I-1582 in birds, wild mammals, fish, aquatic insects and non–arthropod invertebrates. Also, minimal exposure to non-target organisms is anticipated from the proposed use of Votivo 240 FS Nematicide as a seed treatment to suppress root nematodes in soybean and corn seeds.

Value Considerations

What Is the Value of Votivo 240 FS Nematicide?

Votivo 240 FS Nematicide is a microbial seed treatment that suppresses economically important nematode species on corn and soybean.

This product represents the first biological nematicide registered on these field crops. Votivo 240 FS Nematicide constitutes a useful nematode management tool given the increasing nematode populations in Canada as a result of changes in agricultural practices.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures on the label of Votivo 240 FS Nematicide to address the potential risks identified in this assessment are as follows:

Key Risk-Reduction Measures

Human Health

Although the potential for toxicity is low in individuals exposed to *Bacillus firmus* strain I-1582, sensitization may occur upon repeated exposure to high concentrations of the product. A label statement warning users that the product is a potential sensitizer is required. To minimize exposure to mists generated while handling or applying Votivo 240 FS Nematicide, applicators, mixer/loaders, and handlers will be required to wear personal protective equipment, including a long-sleeved shirt, long pants, shoes plus socks, water-proof gloves, and a dust/mist filtering respirator (MSH/NIOSH approval number prefix TC-21C) or a NIOSH approved respirator with any N-95, R-95, P-95 or HE filter for biological products

Environment

As a general precaution, the label prohibits the direct application of the product to aquatic habitats (such as lakes, streams and ponds). The label also directs growers to avoid contaminating surface water by disposal of equipment wash waters.

Other Information

The relevant test data on which the decision is based (as referenced in PRD2011-24, *Bacillus firmus* strain I-1582) are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision, www.hc-sc.gc.ca/cps-spc/pest/part/protect-proteger/publi-regist/index-eng.php#rrd) or contact the PMRA's Pest Management Information Service.

[5] As per subsection 35(1) of the *Pest Control Products Act*.

Appendix I Comments and Responses

1. Comment on label mitigation measures with respect to occupational exposure:

The commenter disagrees with the PMRA's requirement for workers who are treating seeds with Votivo 240 FS to wear dust/mist filtering respirators and the requirement for the precautionary statement, "Potential Sensitizer" on the label for the product.

The commenter believes that the lack of allergenicity observed during the extensive use of the Bacillus genus in a wide range of products with varying degrees of human exposure including a lack of respiratory sensitization incidents associated with the use of *Bacillus firmus* I-1582 in seed treatments in the United States and the fact that the use of *Bacillus firmus* in seed treatment does not produce high levels of respiratory exposure, the sensitization potential of *Bacillus firmus* strain I-1582 is very low and a respirator should not be required.

The commenter also believes that the PMRA could track whether more protective measures are required by evaluating any reports of hypersensitivity incidents associated with products containing *Bacillus firmus* while allowing the use of these products without the need for respirators.

Finally, the commenter recommends the use of the precautionary statement, "Potential Allergen" on the product label instead of "Potential Sensitizer" because the term "sensitizer" can suggest an irritative effect rather than allergic potential.

PMRA Response:

The requirement for a dust/mist filtering respirator (MSH/NIOSH approval number prefix TC-21C) is a standard precautionary measure for microbial pest control products (MPCA) for which there is a potential for inhalation exposure (example, application using commercial mist sprayers). This requirement was largely adopted due to hygienic/sensitization concerns associated with the use of large concentrations of microorganisms.

Microbial pest control products contain numerous biological macromolecules associated with not only the microbial pest control agent, but those associated with possible microbial contaminants, and growth media constituents as well. Many of these biological materials could, in theory, induce allergies in susceptible individuals via a number of possible routes of exposure. The PMRA is aware of standard OECD and USEPA test methods for evaluating the sensitization potential of products and assessed the sensitization study submitted in support of GB-126. However, these methods only measure the sensitization potential of compounds on a limited number of test animals and only via the dermal route. Since this study did not include a larger number of animals to account for natural variation in any given population and only measured the sensitization potential of GB-126 via the dermal route (example, not inhalation or intranasal routes), it does not entirely address PMRA's concerns with the use of Votivo 240 FS Nematicide. Although there have been no reports of respiratory sensitization as a result of the use of *Bacillus firmus* I-1582 in seed treatments in the United States, it was noted that labels for products containing this active ingredient include the requirement for a dust/mist filtering respirator meeting NIOSH standards of at least N-95, R-95 or P-95. Therefore, the PMRA will

maintain the requirement for a dust/mist filtering respirator on the product label as standard personal protective equipment for workers who are treating seeds.

The label statement, "Potential Sensitizer" is a standard precautionary statement for MPCAs. The use of the word "sensitizer" for MPCAs is intended to distinguish the sensitization potential of the active ingredients from other potential allergens which may be present in products as formulants and which are required to be labelled as "allergens". Therefore, revisions to the requirement for the "Potential Sensitizer" precautionary statement on the label for Votivo 240 FS will not be considered by the PMRA at this time.